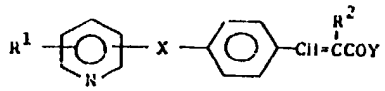
(12) UK Patent Application (19) GB (11) 2 117 760 A

(21) Application No 8304604
(22) Date of filing 18 Feb 1983
(30) Priority data
(31) 57/028392
(32) 24 Feb 1982
(33) Japan (JP)
(43) Application published 19 Oct 1983
(51) INT CL³
C07D 213/62
A61K 31/44
(52) Domestic classification
C2C 1530 200 215 220 221 225 22Y 248 250 251 257 25Y 281 282 29X 29Y 30Y 342 34Y 350 364 366 367 368 36Y 373 37Y 43X 500 50Y 552 574 584 594 613 614 624 628 62X 658 65X 662 672 775 776 802 80Y AA BB KP KQ QS TA
U1S 1320 C2C
(56) Documents cited
None
(58) Field of search
C2C

(71) Applicants
Maruko Seiyaku Co. Ltd., (Japan),
No 5-17 Kodama 1-chome,
Nishi-ku,
Nagoya-shi,
Aichi,
Japan.
(72) Inventors
Sachio Ohno,
Kiyoshi Mizukoshi,
Osamu Komatsu,
Mitsuaki Nagasaka,
Yoshiki Nakamura.
(74) Agent and/or Address for Service
Gee and Co.,
Chancery House,
Chancery Lane,
London WC2A 1QU.

(54) Pyridyl oxy- or thio-phenyl pharmaceutical compounds

(57) Pyridyl compounds are represented by the general formula



(I)

where X is -O- or -S-, R^1 and R^2 each is H or C1-3 alkyl, Y is -OH, $-OR^3$ or $-NR^4R^5$ where R^3 is C1-4 alkyl and R^4 and R^5 each are H or C1-4 alkyl or C3-6 cycloalkyl. Pharmaceutically acceptable salts include acid addition salts and metal salts of the carboxyl group.

Four preparations are described, according to the nature of Y.

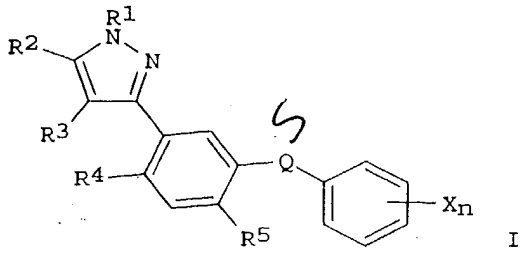
Pharmaceutical compositions contains the compounds for dosage of 0.1 to 60 mg/kg body weight orgally or 0.01 to 4 mg/kg by injection.

The compounds have specific inhibitory activity on thromboxane A_2 biosynthesis and are useful for prevention and treatment of disorders caused by thromboxane A_2, such as thrombosis or cardiac infarction.

GB 2 117 760 A

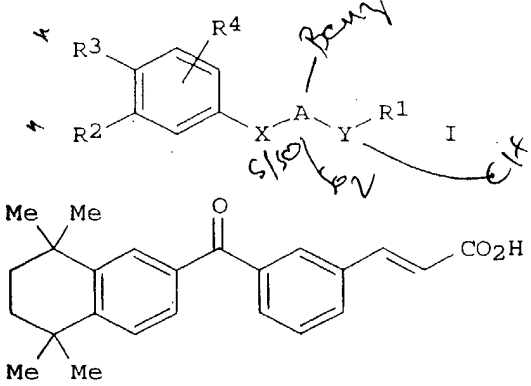
			WO 1999-EP5963 W 19990813
US 6495492	B1	20021217	US 2001-763429 20010220
			DE 1998-19838706A 19980826
			WO 1999-EP5963 W 19990813
US 6559102	B1	20030506	US 2002-279669 20021024
			DE 1998-19838706A 19980826
			WO 1999-EP5963 W 19990813
			US 2001-763429 A320010220

OS MARPAT 132:180568
GI



I

AB Title compds. [I; n = 0-5; Q = O, S, SO, SO2, imino; R1 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl; R2 = (substituted) alkyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonylalkenyl, alkenyloxy, alkenylthio, alkynyl, alkynyloxy, alkynylthio, cycloalkyl, cycloalkylalkyl; R3 = H, halo, (substituted) alkyl; R4 = H, cyano, thiocarbamoyl, halo; R5 = cyano, thiocarbamoyl, halo, (substituted) alkyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl; X = OH, amino, NO2, cyano, CO2H, carbamoyl, thiocarbamoyl, F, Cl, Br, iodo, (substituted) alkyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, etc.], were prepared Thus, Et 2-(4-hydroxyphenoxy)propionate in Me2SO was treated with NaH and then with 4-bromo-3-(4-cyano-2,5-difluorophenyl)-5-difluoromethoxy-1-methyl-1H-pyrazole followed by 2.5 h stirring to give 56% Et 2-[4-[2-cyano-5-[4-bromo-5-(difluoromethoxy)-1-methyl-1H-pyrazol-3-yl]-4-fluorophenoxy]phenoxy]propionate. The latter showed strong herbicidal activity and was well tolerated by crop plants.



I

II

AB The invention concerns novel bi-aromatic compds. I [R1 = Me, CH2OR5, OR5, COR6; Y = (un)substituted CH:CH or C.tplbond.C; A = (un)substituted divalent (ortho or meta) benzene, furan, thiophene, or pyridine nucleus; X = O, S, SO, SO2, CO, C(:CH2), C(:CMe2), CH2, etc.; R2, R3 = H, alkyl, OR5, SR5, polyether; or R2R3 may form ring optionally substituted by Me or interrupted by O or S; R4 = H, halo, alkyl, OR5, polyether; R5 = H, alkyl, acyl; R6 = H, alkyl, (un)substituted NH2 or OH]. The compds. are agonists or antagonists of RXR receptors (no data), and can be used in pharmaceutical compns. for human or veterinary medicine (in particular for treating dermatol., rheumatic, respiratory, cardiovascular, and ophthalmol. disorders), as well as cosmetic compns. For instance, Friedel-Crafts acylation of 5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalene with 3-iodobenzoyl chloride (54.6%), followed by Pd-catalyzed vinylation of the iodide with Me acrylate (77%), and hydrolysis of the resultant ester with aqueous NaOH in THF (86%), gave title compound II.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

direct bond; X1 = O, S, SO, SO2, a direct bond; Y = a direct bond, lower alkylene, lower alkylidene; Z = COOH, 5-tetrazolyl, HOCH2, carboxyl derivatized in the form of a pharmaceutically acceptable ester], useful as LTB-4 antagonists, were prepared Thus, treatment of a solution of (E)-[5-(2-diethylcarbamoyl-1-methylvinyl)-2-(2,6-difluorobenzyloxy)phenyl]acetaldehyde (preparation described) and 2M isobutylene/THF in tBuOH with a solution of NaClO2 and NaH2PO4.H2O in H2O afforded the title compound (E)-II which showed IC50 of 87 nM against LTB-4 binding.

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT